Spearman Simultaneous Estimation for a Compartmental Model

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SPEARMAN SIMULTANEOUS ESTIMATION

FOR A COMPARTMENTAL MODEL*

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SUMMARY

A compartmental model is presented for tracer experiments with a fixed and known amount of tracer material which is injected initially into a single compartment and accumulates in another compartment. The model could also arise as a description of chemical reactions. The model is represented as a system of linear combinations of exponentials with common exponential parameters. Then a simultaneous estimation procedure, which is a generalization of the Spearman estimation procedure presented by Johnson and Brown [1961] for a single equation, is developed for this model under the assumption that the values of the independent variable in the model are equally spaced on a logarithmic scale. Asymptotic properties of the estimation procedure are investigated and an example is given.

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INTRODUCTION

Data from tracer experiments often are represented by the model

$$Y_{ij} = \sum_{k=1}^{n} \alpha_{ik} e^{-\lambda_{k} x_{j}} + \alpha_{i,n+1} + \epsilon_{ij}, \qquad (1.1)$$

where Y_{ij} and ε_{ij} represent random variables associated with the j^{th} observation on the i^{th} equation, $i=1,2,\ldots,n,x_j$ represents an independent variable, and the α_{ik} 's and λ_k 's are parameters inherent in the experimental situation. This model, with certain relationships specified among the α_{ik} coefficients, is presented in Section 2 for tracer experiments which can be represented by a compartmental model with a fixed and known amount of tracer which is injected into the first compartment initially and then accumulates in a second compartment. In Section 3 an estimation procedure is developed for this tracer experiment model when the x_j 's are equally spaced on a logarithmic scale. Although the model is developed for tracer experiments here, it could also arise, for instance, as a model for chemical reactions such as those discussed by Box and Draper [1965].

Since the exponential parameters $\lambda_1,\lambda_2,\ldots,\lambda_n$ appear in each one of the regression equations of (1.1), we make use simultaneously of all of the observations on all of the equations being studied to estimate these parameters. Beauchamp and Cornell [1966], Turner et al [1963], and Zellner [1962] present simultaneous least squares estimation procedures. However, Zellner considers only linear regression equations, Turner et al assume that the covariance matrix of the ϵ_{ij} is known, and the procedures in Turner et al, and Beauchamp and Cornell, are often difficult to compute. Therefore the procedure presented here provides a simple alternative to the least squares procedures or can be used to compute initial estimates for such procedures. The estimation procedure presented in

Section 3 is a generalization of the Spearman estimation technique presented by Johnson and Brown [1961], who considered the estimation problem for n=1 and $\alpha_{10} = -\alpha_{11} = 1$ in equation (1.1), that is, for a single equation simple exponential regression model. In Section 4 some of the asymptotic properties of the estimators found by the procedure developed in Section 3 are stated. An example showing the application of the procedure for a particular regression model is given in Section 5.

2. MODELS

The use of radioactive tracer material is an example of an experimental situation which yields data that may be described by the set of regression equations given by (1.1). Berman and Schoenfeld [1956] and Sheppard [1962] have discussed the formulation of mathematical models for such experiments. In a biological experiment these formulations represent an organism by several chemical states or sites of a physiological substance designated as compartments. It is assumed that there are fixed transition probabilities or turnover rates from one compartment to another, and the whole system is assumed to be in steady state. The turnover rates are also assumed to be proportional to the amounts of material in the compartments. The mammillary and catenary systems are two examples of compartmentalized systems in steady state and Sheppard [1962] gives a detailed discussion of these systems. These models may be formally described as follows:

(1) The catenary system involves (n+1) compartments that may be thought of as arranged in a chain-like manner where each compartment has non-zero transition rates only with the compartments adjacent to it.

(2) The mammillary system involves n peripheral compartments that have turnover rates with a central compartment but no turnover between the n peripheral compartments.

If we want to consider the expected values of our observations as being continuous functions of the independent variable, then we denote this by writing x in place of x_j , that is, x denotes any arbitrary value and x_j represents a particular fixed value. From the discussion in the preceding paragraphs, the following set of differential equations is formed to describe the general (n+1) - compartmental problem:

$$\frac{dE[Y_{i}(x)]}{dx} = -\tau_{ii}E[Y_{i}(x)] + \sum_{\substack{h=1\\h\neq i}}^{n+1}\tau_{ih}E[Y_{h}(s)]$$
(2.1)

for i=1,2,...,n+1, where $E[Y_i(x)]$ is the expected amount of labeled material in the ith compartment at time x, τ_{ih} is the fractional amount of material in the hth compartment flowing to the ith compartment per unit time, and

$$\tau_{ii} = \frac{n+1}{\sum_{h=1}^{\infty} \tau_{hi}}$$

$$h \neq i$$

Berman and Schoenfeld [1956] show that the solution to (2.1) is

$$E[Y_{i}(x)] = \sum_{k=1}^{n+1} \alpha_{ik} e^{-\lambda_{k} x}$$
(2.2)

for i=1,2,...,n+1, where the coefficients α_{ik} are functions of the τ_{ih} and the initial conditions of the experiment. Let τ be an (n+1) \times (n+1) matrix whose diagonal elements are given by τ_{ii} and off diagonal elements are given by - τ_{ih} . Then $\lambda_1, \lambda_2, \ldots, \lambda_{n+1}$ are the characteristic roots of τ . Throughout this paper we assume that the characteristic roots of τ are real and distinct.

From equation (2.2) we note that the number of exponential terms in each

equation is determined by the number of nonzero characteristic roots of τ , which is either n or n+1 when these roots are distinct and which is also equal to the rank of τ . By investigating the matrix τ for the general (n+1) - compartment catenary and mammillary systems, we can show that the rank of τ is equal to n, so exactly one λ , say λ_{n+1} , is zero. In addition, when the amount of tracer material in the system is fixed and known, we can express the system of equations given in equation (2.2) in terms of new quantities which represent the proportions of labeled material in the compartments at time x. In this instance there are only n independent equations in (2.2) since

$$\begin{array}{l}
n+1 \\
\Sigma \\
i=1
\end{array}$$

$$E[Y_i(x)]$$

is fixed for all x. We also impose the following conditions: (1) $E[Y_1(0)] = E[Y_2(+\infty)] = 1$ and (2) $E[Y_1(+\infty)] = E[Y_2(0)] = 0$, which would be satisfied by an (n+1) - compartment catenary or mammillary system where a fixed amount of tracer material is injected into the first compartment of the system and is allowed to accumulate in the second compartment of the system. We may now combine the above discussion into the following theorem:

Theorem 1: The regression model used to describe the general (n+1) - compartment catenary or mammillary systems, when a fixed and known amount of tracer material is injected into the first compartment and accumulates in the second compartment of the system, is given by the model in equation (1.1) with the following relations satisfied by the coefficients of (1.1):

(1)
$$\alpha_{1,n+1} = 0$$
; $\alpha_{1n} = 1 - \alpha_{11} - \alpha_{12} - \dots - \alpha_{1,n-1}$,

(2)
$$\alpha_{2,n+1} = 1$$
; $\alpha_{2n} = -(\alpha_{21} + \alpha_{22} + \dots + \alpha_{2,n-1} + \alpha_{2,n+1})$
= $-(1 + \alpha_{21} + \dots + \alpha_{2,n-1})$,

(3)
$$\alpha_{i,n+1} = 0$$
 for $i=3,4,...,n$,

(4)
$$\alpha_{in} = -(\alpha_{i1} + \alpha_{i2} + ... + \alpha_{i,n-1})$$
 for i=3,4,...,n.

During the development of the estimation procedure given in the next section, the only assumption that we need to make about the random variables ϵ_{ij} is that $E(\epsilon_{ij}) = 0$ for all i and j. However, additional assumptions are needed in order to investigate some of the asymptotic properties of the estimators found by this procedure and these assumptions are given in Section 4.

3. GENERALIZED SPEARMAN ESTIMATION

In this section we develop an estimation procedure for equally spaced x values on a logarithmic scale, which is a generalization of the Spearman estimation procedure presented by Johnson and Brown [1961], to estimate the parameters in the regression model given in Theorem 1. We assume here that the independent variable is of the form $x = \exp(z)$. From Theorem 1 we note that the regression equations of our model are of two different types:

$$E[Y_{i}(z)] = \sum_{k=1}^{n-1} \alpha_{ik} \exp(-\lambda_{k} e^{z}) + (1-\alpha_{i1}-...-\alpha_{i,n-1}) \exp(-\lambda_{n} e^{z}) , \qquad (3.1)$$

i=1,2;

$$E[Y_i(z)] = \sum_{k=1}^{n-1} \alpha_{ik} \exp(-\lambda_k e^z) - (\alpha_{i1} + \dots + \alpha_{in-1}) \exp(-\lambda_n e^z) , \qquad (3.2)$$

i=3,4,...,n. Then consideration of equation (3.1) and the integral

$$\mu_{\mathbf{i}}^{(s)} = \int_{-\infty}^{\infty} dE[Y_{\mathbf{i}}(z)], \qquad (3.3)$$

for s=1,2,...,n, leads, after extensive algebra, to the relationship

$$K_{i,n-1}^{\Lambda_1 + K_{i,n-2}^{\Lambda_2 + K_{i,n-3}^{\Lambda_3 + \dots + K_{i1}^{\Lambda_{n-1} - \Lambda_n} = -K_{in}},$$
 (3.4)

i=1,2, where

$$K_{i1} = \mu_{i}^{(1)} + I_{1}$$

$$K_{i2} = \mu_{i}^{(2)} + I_{2} - 2I_{1}K_{i1}$$

$$\vdots$$

$$K_{in} = \mu_{i}^{(n)} + I_{n} - \binom{n}{1}I_{n-1}K_{i1} - \binom{n}{2}I_{n-2}K_{i2} - \cdots - \binom{n}{n-1}I_{1}K_{i,n-1},$$

$$I_{h} = \int_{0}^{\infty} (\ln t)^{h} e^{-t} dt, h=1,2,...,n,$$

and the Λ_r , r=1,2,...,n, are the n elementary symmetric functions of the $\ln \lambda_k$. That is, Λ_r equals the sum of all possible products of the terms $\ln \lambda_k$ taken r at a time. Also, equations (3.2) and (3.3) can be used to show that

$$K_{i,n-1}^{\dagger} \Lambda_{1}^{\dagger} + K_{i,n-2}^{\dagger} \Lambda_{2}^{\dagger} + \dots + K_{i2}^{\dagger} \Lambda_{n-2}^{\dagger} + K_{i1}^{\dagger} \Lambda_{n-1}^{\dagger} = K_{in}^{\dagger}$$
, (3.5)

i=3,4,...,n, where

$$K_{i1}^{!} = \mu_{i}^{(1)}$$

$$K_{i2}^{!} = \mu_{i}^{(2)} - 2I_{1}K_{i1}^{!}$$

$$\vdots$$

$$K_{in}^{!} = \mu_{i}^{(n)} - \binom{n}{1}I_{n-1}K_{i1}^{!} - \binom{n}{2}I_{n-2}K_{i2}^{!} - \cdots - \binom{n}{n-1}I_{1}K_{i,n-1}^{!}$$

and I_h and Λ_r are defined above. The detailed algebra leading to (3.4) and (3.5) is given by Beauchamp [1966].

From the set of linear equations in the Λ_r 's given by (3.4) and (3.5), we solve for the quantities $\Lambda_1, \Lambda_2, \ldots, \Lambda_n$ in terms of the K's and K's. Using

these solutions we proceed to solve for $\ln \lambda_1, \ln \lambda_2, \ldots, \ln \lambda_n$, by applying the same technique as discussed by Cornell [1962], that is, we obtain the n roots of the polynomial

$$w^{n} - \Lambda_{1}w^{n-1} + \Lambda_{2}w^{n-2} - \dots + (-1)^{n-1}\Lambda_{n-1}w + (-1)^{n}\Lambda_{n} = 0.$$
 (3.6)

These roots, say \mathbf{w}_k , $k=1,2,\ldots,n$, are related to the λ_k parameters by $\lambda_k = \exp(\mathbf{w}_k)$, where the ordering of the λ_k 's is arbitrary. We note that the solutions for λ_k , $k=1,2,\ldots,n$, are functions of the K's and K''s, which, in turn, are functions of known constants and the unknown quantities $\mu_i^{(s)}$ for i, $s=1,2,\ldots,n$. Hence, in order to obtain estimators of the exponential parameters we need only to propose estimators for the $\mu_i^{(s)}$.

The observations for each regression equation of our model are taken in a manner similar to that discussed by Johnson and Brown [1961], that is, for an odd number of observations the values of the independent variable are given by $z_j = z_0 + jd$ where $j=0,\pm 1,\pm 2,\ldots,\pm M$, and for an even number of observations the values of the independent variable are given by $z_j = z_0 + d(j+\frac{1}{2})$ for $j=0,\pm 1,\pm 2,\ldots,\pm M$, the value of the j observation on the j observation. Then by considering the definition of a Riemann-Stieltjes integral, we take as an estimator of $\mu_j^{(s)}$ the sum

$$\hat{\mu}_{i}^{(s)} = \sum_{j=-M}^{N-1} \left(\frac{z_{j}+z_{j+1}}{2}\right)^{s} \Delta y_{ij}, \qquad (3.7)$$

where $\Delta y_{ij} = y_{i,j+1} - y_{ij}, z_j$ has been defined earlier, and N=M-1 if an even number of observations is taken and N=M if an odd number of observations is taken. We assume that M is large enough so that $y_{i,-M} = E[Y_i(-\infty)]$ and $y_{i,N} = E[Y_i(\infty)]$.

Then by using the estimators of $\mu_i^{(s)}$ given by (3.13) in the expressions for the K's and K's, we obtain our estimators of the λ_i , k=1,2,...,n.

Next we want to estimate the coefficients or linear parameters in our regression model. To obtain these estimators we substitute the estimators of the $\lambda_{\rm L}$, found by the generalized Spearman estimation procedure described above, into our set of n independent regression equations. After doing this we have a set of n regression equations which are linear in the unknown coefficients α_{ik} . Therefore, to estimate these coefficients we use the weighted least squares procedure as given by Zellner [1962] if it is reasonable to assume that the covariance matrix of the random variables ϵ_{ij} is known apart from a constant multiplier. Otherwise, we apply a weighted least squares procedure using an estimated covariance matrix as discussed by Beauchamp and Cornell [1966] and Telser [1964]. So our estimation procedure involves two main steps: (1) the estimation of the exponential or nonlinear parameters by a generalized Spearman estimation procedure; and (2) the estimation of the coefficients or linear parameters by a weighted least squares procedure after substituting the estimates of the nonlinear parameters into the regression equations. In most tracer experiments estimation of the exponential parameters is of primary importance so that only the first step might be completed.

4. EVALUATION OF THE ESTIMATORS

In order to apply the estimation procedure developed in Section 3, we need only assume that $E(\epsilon_{ij}) = 0$ for all i and j and that M is large enough so that $y_{i,-M} = E[Y_i(-\infty)]$ and $y_{iN} = E[Y_i(\infty)]$ for all i. The consistency of the estimators of the exponential parameters can be shown under the following additional assumptions:

(1) For fixed i, the random variables ϵ_{ij} , where i=1,2,...,n and j=0,±1,±2,...,±M

or j=0,±1,±2,...,±(M-1),-M, are uncorrelated with finite variance such that $Var(\epsilon_{iM})$ tends to zero as M $\rightarrow \infty$.

- (2) For $i \neq u$ and $j \neq v$, the random variables ϵ_{ij} and ϵ_{uv} are uncorrelated.
- (3) For i, s=1, 2, ..., n,

$$\lim_{M \to \infty} \operatorname{Var}(\hat{\mu}_{i}^{(s)})$$

exists and equals zero.

(4) For all $j, d=z_{j+1}-z_j$ is such that $\lim_{M \to \infty} d = 0$ and $\lim_{M \to \infty} dM = \infty$.

The consistency of the estimators of the exponential parameters is demonstrated by Beauchamp [1966] by considering the estimators as functions of the $\hat{\mu}_i^{(s)}$ estimators defined in (3.7), and applying the definition of a Riemann-Stieltjes integral and a form of Tchebycheff's theorem given by Cramer [1946]. Using the same set of assumptions, it can also be shown that the estimators of the linear parameters are also consistent if these estimators are continuous functions of the $\hat{\lambda}_k$'s, the estimators of the exponential parameters, and if the covariance matrix of the ϵ_{ij} 's is specified apart from a constant multiplier or is replaced by a consistent estimator in the weighted least squares calculations.

If $\hat{\lambda}$ represents the n × 1 vector of estimators of the exponential parameters whose true values are given by the vector λ , then it can be shown that as M $\rightarrow \infty$, $(\hat{\lambda}-\lambda)/[d^3(\text{M+N-2})]^{\frac{1}{2}}$ has a limiting multivariate normal distribution under the assumptions stated at the beginning of this section plus the additional assumption that the elements of $\hat{\lambda}$ have continuous second order derivatives of every kind with respect to the elements of $\hat{\mu}_{*}^{(*)}$, where $\hat{\mu}_{*}^{(*)} = (\hat{\mu}_{1}^{(1)}, \dots, \hat{\mu}_{1}^{(n)}, \hat{\mu}_{2}^{(1)}, \dots, \hat{\mu}_{2}^{(n)}, \dots, \hat{\mu}_{n}^{(n)}, \dots, \hat{\mu}_{n}^{(n)})^{T}$ and the superscript T represents the transpose of a vector. The mean vector of this limiting distribution is shown to be equal to the zero vector and the covariance matrix is given by

$$\lim_{M \to \infty} \left(\frac{1}{d^3(M+N-2)} \right) FE(\epsilon_* \epsilon_*^T) F^T$$

where d,M, and N are defined in Section 3, $\epsilon_{\star} = \hat{\mu}_{\star}^{(\star)} - E(\hat{\mu}_{\star}^{(\star)})$, $F = (F_1^T, F_2^T, \dots, F_n^T)^T$, and

$$\mathbf{F}_{k} = \left(\frac{\partial \hat{\lambda}_{k}}{\partial \hat{\mu}_{1}^{(1)}}, \dots, \frac{\partial \hat{\lambda}_{k}}{\partial \hat{\mu}_{1}^{(n)}}, \dots, \frac{\partial \hat{\lambda}_{k}}{\partial \hat{\mu}_{n}^{(1)}}, \dots, \frac{\partial \hat{\lambda}_{k}}{\partial \hat{\mu}_{n}^{(n)}}\right)$$

evaluated at the point $\hat{\mu}_{*}^{(*)} = \mu_{*}^{(*)}$ for k=1,2,...,n. Each entry in this covariance matrix exists under the assumptions given above. The details of this demonstration are also given by Beauchamp [1966].

5. EXAMPLE

In this section we apply the estimation technique developed in Section 3 to the set of data given in Table 1. These data have been generated for a compartmental model represented by the following diagram for a tracer experiment:

$$\begin{bmatrix} \frac{1}{3} & \frac{\tau_{23}}{2} & \frac{1}{2} \end{bmatrix}$$

The experiment could consist of a test of the rapidity with which particulate contamination is removed from a horizontal laminar flow clean room. Compartment 3 would represent a site near the wall where the air stream enters the laminar flow room, while Compartments 2 and 1 would represent sites in the middle and at the exhaust end of such a room, respectively. Contaminants would be released in Compartment 3 and the relative amount of contamination in each of the compartments would be determined at time intervals equally spaced on a logarithmic scale.

We now note that we have brought this example into the same framework as the general compartmental problem discussed in Section 2. Therefore we have a system of differential equations corresponding to those given in equation (2.1) for n=2. For this particular example let $E[Y_i(x)]$, i=1,2,3, represent the expected proportion of contamination present at time x in the ith compartment. The following boundary conditions are satisfied:

$$E[Y_3(x)] = 1$$
 and $E[Y_2(x)] = E[Y_1(x)] = 0$ at $x = 0$.

TABLE 1 --Data to be fitted by generalized Spearman estimation procedure

j	* _j	z j	yĺj	y _{2j}
-5	1/4	-1.38630	1.00000	0.00000
-4	$\frac{1}{2}$	-0.69315	0.92696	0.01463
-3	1	0	0.87213	0.02986
-2	2	0.69315	0.75029	0.04675
-1	4	1.38630	0.60339	0.10608
0	8	2.07945	0.37711	0.16495
1	16	2.77260	0.18042	0.19098
2	32	3.46575	0.05943	0.14191
3	64	4.15890	0.02628	0.09154
4	128	4.85205	0.00000	0.00000

Corresponding to equation (2.2) we have the following system of equations:

$$\begin{split} & \mathbb{E}[Y_{1}(\mathbf{x})] = \alpha_{11} e^{-\lambda_{1} x} + \alpha_{12} e^{-\lambda_{2} x} + \alpha_{13} e^{-\lambda_{3} x}, \\ & \mathbb{E}[Y_{2}(\mathbf{x})] = \alpha_{21} e^{-\lambda_{1} x} + \alpha_{22} e^{-\lambda_{2} x} + \alpha_{23} e^{-\lambda_{3} x}, \\ & \mathbb{E}[Y_{3}(\mathbf{x})] = \alpha_{31} e^{-\lambda_{1} x} + \alpha_{32} e^{-\lambda_{2} x} + \alpha_{33} e^{-\lambda_{3} x}, \end{split}$$
 (5.1)

where $\lambda_1 = \tau_{23}, \lambda_2 = \tau_{12}, \lambda_3 = 0, \alpha_{11} = -\tau_{12}/(\tau_{12} - \tau_{23}), \alpha_{12} = 1 - \alpha_{11}, \alpha_{13} = 1,$ $\alpha_{21} = -\alpha_{22} = \tau_{23}/(\tau_{12} - \tau_{23}), \alpha_{23} = \alpha_{32} = \alpha_{33} = 0, \text{ and } \alpha_{31} = -\tau_{23}.$ We have the restriction that

$$\begin{array}{l}
3 \\
\Sigma \\
i=1
\end{array} E[Y_{i}(x)] = 1$$

for all x. Hence there are only two independent equations in (5.1), which we take to be the first two. If we let $\alpha_1 = -\alpha_{11}$, $x = \exp(z)$, and $E[Y_1^!(x)] = 1-E[Y_1(x)]$, then the equation for $E[Y_1^!(x)]$ becomes

$$E[Y_1^{t}(z)] = \alpha_1 \exp(-\lambda_1 e^z) + (1-\alpha_1) \exp(-\lambda_2 e^z),$$
 (5.2)

which is of the same form as equation (3.1). In addition, if we let $\alpha_2 = \alpha_{21}$, then the equation for $E[Y_2(x)]$ is given by

$$\mathbf{E}[\mathbf{Y}_{2}(\mathbf{z})] = \alpha_{2} \exp(-\lambda_{1} e^{\mathbf{z}}) - \alpha_{2} \exp(-\lambda_{2} e^{\mathbf{z}}), \qquad (5.3)$$

which is of the same form as equation (3.2).

By using the techniques presented in Section 3, we arrive at the system of equations corresponding to (3.4) and (3.5) given by

$$K_{11}^{\Lambda}_{1} - \Lambda_{2} = -K_{12}$$
,
 $K_{21}^{I}_{1} = -K_{22}^{I}$, (5.4)

where $\Lambda_1 = \ell n \lambda_1 + \ell n \lambda_2$; $\Lambda_2 = \ell n \lambda_1 \ell n \lambda_2$; $K_{11} = \mu_1^{(1)} + I_1$; $K_{12} = \mu_1^{(2)} + I_2 - 2I_1 K_{11}$; $K_{21}^! = \mu_2^{(1)}$; $K_{22}^! = \mu_2^{(2)} - 2I_1 K_{21}^!$; $I_1 = \int_0^\infty (\ell n t) e^{-t} dt$; and $I_2 = \int_0^\infty (\ell n t)^2 e^{-t} dt$. The estimates of $\mu_1^{(1)}$, $\mu_1^{(2)}$, $\mu_2^{(1)}$, and $\mu_2^{(2)}$ for this particular example are given by $\hat{\mu}_2^{(1)} = -1.59148$; $\hat{\mu}_1^{(2)} = -4.28851$; $\hat{\mu}_2^{(1)} = -0.54531$; and $\hat{\mu}_2^{(2)} = -2.65392$. Substituting these values into the expressions for the K's and K''s, the system of equations given in (5.4) becomes

$$-2.16870L_{1}-L_{2} = 4.81403,$$

$$-0.54531L_{1} = 3.28345,$$
(5.5)

where L_1 and L_2 are the estimates of Λ_1 and Λ_2 , respectively. Solving (5.5), we find L_1 = -6.02125 and L_2 = 8.24425. In order to obtain the estimates of $\ell n \lambda_1$ and $\ell n \lambda_2$ we calculate the roots of the following quadratic equation:

$$w^2 + 6.02125w + 8.24425 = 0.$$
 (5.6)

The roots of (5.6) are given by $w_1 = -3.91595$ and $w_2 = -2.10530$. We take $\hat{\lambda}_k = \exp(w_k)$, so our estimates of λ_1 and λ_2 are $\hat{\lambda}_1 = 0.01990$ and $\hat{\lambda}_2 = 0.12131$, respectively.

The next step in our estimation procedure is to estimate the linear parameters, α_1 and α_2 , in equations (5.2) and (5.3). The observations in Table 1 were generated by adding random normal deviates to calculated expected

values and taking $E(\epsilon_{1j}^2) = P_{1j}(1-p_{1j})/m$, $E(\epsilon_{2j}^2) = P_{2j}(1-p_{2j})/m$, and $E(\epsilon_{1j}\epsilon_{2j}) = -p_{1j}p_{2j}/m$, where $P_{1j} = E[Y_1(z_j)]$, $P_{2j} = E[Y_2(z_j)]$, and $P_{2j} = E[Y_2(z_j)]$.

$$Y_{1}'(z_{j}) - \exp(-\lambda_{2}e^{z_{j}}) = \alpha_{1}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{2}e^{z_{j}})] + \alpha_{1}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{2}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{2}e^{z_{j}})]] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})]] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})]] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})]] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{z_{j}})] + \alpha_{2}[\exp(-\lambda_{1}e^{z_{j}}) - \exp(-\lambda_{1}e^{$$

If λ_1 and λ_2 were known, then the usual weighted least squares estimators of α_1 and α_2 would be given by

$$\hat{\alpha}_{\star} = (D_{Z}^{T} \Omega^{-1} D_{Z})^{-1} (D_{Z}^{T} \Omega^{-1} y_{\star}) = (\hat{\alpha}_{1}, \hat{\alpha}_{2})^{T};$$

$$D_{Z} = \begin{pmatrix} Z & 0 \\ 0 & Z \end{pmatrix};$$

$$Z = \begin{pmatrix} \exp(-\lambda_{1} e^{z^{2} - 4}) & -\exp(-\lambda_{2} e^{z^{2} - 4}), \dots, \exp(-\lambda_{1} e^{z^{3}}) & -\exp(-\lambda_{2} e^{z^{3}}) \end{pmatrix}^{T};$$

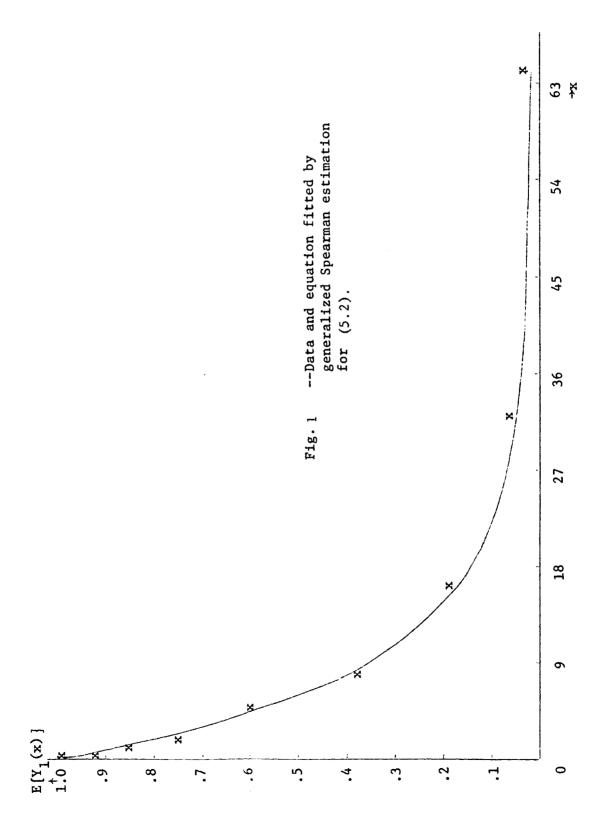
$$(5.8)$$

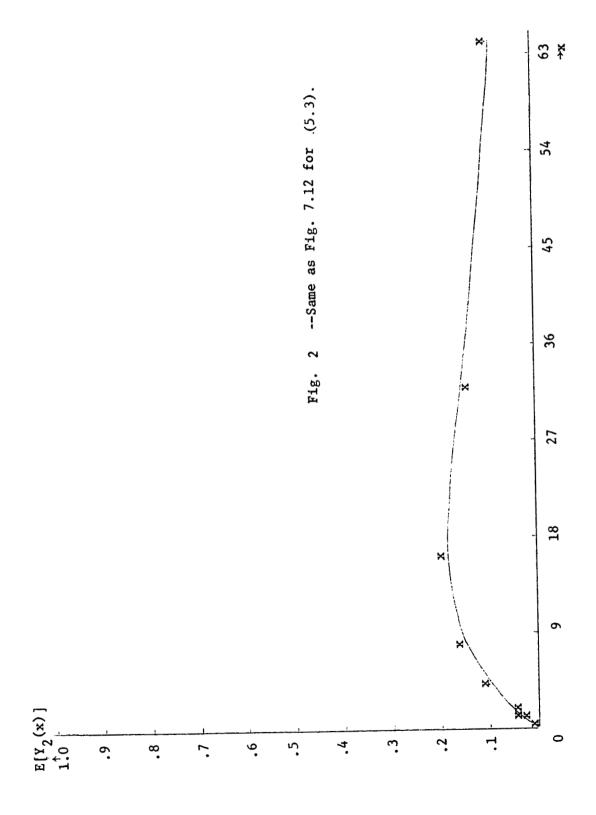
 Ω is the covariance matrix of the random variables $\epsilon_{\mbox{ij}};$

$$y_* = (y_{1,-4} - \exp(-\lambda_2 e^{z_{-4}}), \dots, y_{1,3} - \exp(-\lambda_2 e^{z_{3}}), y_{2,-4}, \dots, y_{23})^T;$$

and y_{ij} represents the jth observation on the ith equation. We now substitute the estimates $\hat{\lambda}_1$ and $\hat{\lambda}_2$ into equation (5.8) giving us the estimates of the

parameters α_1 and α_2 , denoted by $\hat{\alpha}_1 = 0.05501$ and $\hat{\alpha}_2 = 0.30899$, respectively. Graphs showing the original data (x) with the fitted regression equations of our model are given in Figures 1 and 2.





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